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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/757,981	01/13/2004	Steven B. Landau	3506.1001-002	4256

21005 7590 03/30/2006

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EXAMINER	
GRAFFEO, MICHEL	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 03/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/757,981	LANDAU ET AL.	
	Examiner	Art Unit	
	Michel Graffeo	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-21 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-21 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 3/22/04 3/3/04 5/3/04 12/8/04 1/26/05 3/1/06
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I in the reply filed on 1 March 2006 is acknowledged.

Claims 22-70 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim.

Status of Action

Claims 1-21 are pending and examined.

Claim Rejections - 35 USC § 112 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 7-16 and 21 are rejected under 35 U.S.C. 112, first paragraph, because the specification coupled with the prior art (see Turconi et al.), while being enabling for a method of treating nausea etc. when such is induced by cisplatin for example or a cause with a related mechanism where the treatment ends at a reduction in emetic episodes, does not reasonably provide enablement for the treatment of

nausea, vomiting etc. from all sources, such as for example, vomiting associated with eating disorders or muscle paralysis for example, nor for the treatment without any specified endpoint. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

In this regard, the application disclosure and claims have been compared per the factors indicated in the decision *In re Wands*, 8 USPQ2nd 1400 (Fed. Cir. 1988) as to undue experimentation.

The factors include:

1) the nature of the invention;
2) the breadth of the claims;
3) the predictability or unpredictability of the art;
4) the amount of direction or guidance presented;
5) the presence or absence of working examples;
6) the quantity of experimentation necessary;
7) the state of the prior art; and ,
8) the relative skill of those skilled in the art.

Each factor is addressed below on the basis of comparison of the disclosure, the claims and the state of the art in the assessment of undue experimentation.

1) the nature of the invention; the invention is directed to a method of treating vomiting, nausea etc. associated with every and all cause but has not recited the step(s) that (a) result in preventing nor (b) have a specified end result of the treatment.

2) the breadth of the claims; the scope of the method claims includes the the treatment of nausea, vomiting etc. associated with all causes.

3) the predictability or unpredictability of the art; the ability of treating nausea, vomiting etc. from all sources, is not yet known in the art. See http://www.eating-disorders.org.uk/ retrieved 25 March 2006 which explains that eating disorders, such as compulsive or binge eating, anorexia, bulimia and dieting failure affect millions of people in every walk of life. The overview continues to explain how people are attempting to control or treat eating disorders by dieting, fasting, over-exercising, using slimming pills, diuretics, laxatives and purging, suggesting that at the present time, there are no efficacious treatments and that these strategies can produce short term weight control, but they do not provide an answer to eating disorders and can often make things even worse because the underlying problem needs to be addressed. With thousands of people suffering from eating disorders, harbouring persistent weight problems and obsessed with food and weight it can be concluded that there is still unpredictability in the at regarding vomiting caused by eating disorders.

The burden of enabling one skilled in the art to treat nausea, vomiting etc. from all sources would be much greater than that of enabling the treatment of such diseases. In the instant case, the specification does not provide guidance as to how one skilled in the art would accomplish the objective of treating nausea, vomiting etc. from all sources. Nor is there any guidance provided as to a specific protocol to be utilized in order to show the efficacy of the presently claimed active ingredients for treating vomiting caused by eating disorders for example.

No experimental evidence supporting the contention that the claim specified actives would actually treat these diseases by simply administering the claim specified active agents has not been demonstrated nor practice the invention without an envisaged endpoint or result of the treatment (note the absence of such recitation in the current claim(s)). The specification fails to enable one of ordinary skill in the art to practice the presently claimed method for treating and for practicing same without a specific endpoint for the treatment of the claimed diseases.

4) the amount of direction or guidance presented; the specification does not provide any guidance in terms of preventing cancer.

5) the presence or absence of working examples; no working examples are provided for treating nausea, vomiting etc. from all sources, for example in a patient, in the specification. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

6) the quantity of experimentation necessary; the quantity of experimentation would be undue to one of skill in the art and amount to the trial and error type of experimentation without a priori expectation of success. Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims. To support a claim to the treatment of

nausea, vomiting etc. from all sources or the like, Applicant would need to provide confirmative in vivo data supporting the prevention of the disease as well as a method and dosage regime resulting in the prevention of same.

In view of the breadth of the claims, the chemical nature of the invention and unpredictability of preventing caner, and the lack of working examples regarding the activity as claimed, one skilled in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

In consideration of each of factors 1-6, it is apparent that there is undue experimentation because of variability in prediction of outcome that is not addressed by the present application disclosure, examples, teaching and guidance presented. Absent factual data to the contrary, the amount and level of experimentation needed is undue.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wu et al. Effects of acute and chronic administration of MCI-225, a new selective noradrenaline reuptake inhibitor with 5-HT3 receptor blocking action, on extracellular noradrenaline levels in the hypothalamus of stressed rats. Japanese Journal of Pharmacology (2000), 83(1), 31-38 in view of US Patent No. 5,223,511 to Turconi et al. (cited to show the status of art).

Wu et al. teach that MCI-225, the compound of claim 1, blocks inhibits serotonin and teaches an oral dosage of 3 or 10 mg/kg which for a .25kg mouse equates to less than 10mg (in current claims 1-21; see Abstract).

Wu et al. do not teach that MCI-225, a 5-HT_3 inhibitor, can be used for a method of treating emesis.

Turconi et al. teach that 5-HT antagonists may be particularly useful in the treatment of chemotherapy induced nausea and emesis as well as nausea caused by radiation, motion sickness, headaches, motion sickness (in current claims 1-21; see col 1 lines 35-40). Although Turconi et al. do not specifically recite that 5-HT antagonists are useful in treating nausea caused by a specific medicine, one of ordinary skill in the art would have found that obvious in light of the long list of causes and that the cause, having the same trigger as a listed cause, would not make the claim patentably distict.

Although Turconi et al. is cited to show the level of knowledge in the art, one of ordinary skill in the art would have been motivated to combine the above references and as combined would teach the invention as claimed. One of ordinary skill in the art would have been motivated to combine the references because both are directed to serotonin or 5-HT receptor antagonists and the therapeutic uses therefor. Also, 5-HT receptor antagonists are known and currently marketed for the treatment of emesis, for example Zofran® Kytril® and Anzemet®. Therefore, one of ordinary skill in the art would have expected efficacy during treatment of nausea with the known 5-HT receptor antagonist. Thus, the combined references teach and make prima facie obvious how to use the claimed invention at the time that it was made.

Double Patenting

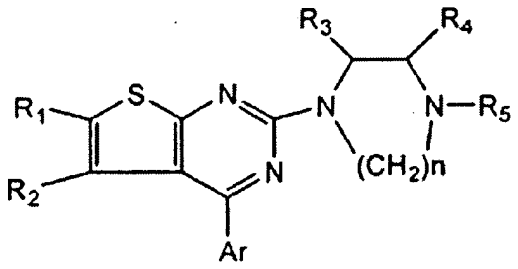
The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-21 are provisionally rejected on the ground of nonstatutory double patenting over claims 71-158 of copending Application No. 10/846978. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

The subject matter claimed in the instant application is fully claimed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter, as follows: A method for the treatment of nausea and vomiting comprising the following compound:



Claims 1-21 are provisionally rejected on the ground of nonstatutory double patenting over claims 71-158 of copending Application No. 10/846979. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

The subject matter claimed in the instant application is fully claimed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter, as follows: A method for the treatment of nausea and vomiting in a patient suffering therefrom, comprising administering to the patient an effective amount of 4-(2-fluorophenyl)-6-methyl-2-(1-piperazinyl)thieno[2,3-D]pyrimidine or a salt thereof.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michel Graffeo whose telephone number is 571-272-8505. The examiner can normally be reached on 9am to 5:30pm Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

27 March 2006
MG

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